PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/051051	07.06.2004	05.03.2004

International Patent Classification (IPC) or both national classification and IPC
G01N27/08, G01N27/447, G01N30/64

Applicant
AGILENT TECHNOLOGIES, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/051051

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/051051

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	6-12,29
	No:	Claims	1-5,13-28
Inventive step (IS)	Yes:	Claims	6-8,29
	No:	Claims	1-5,9-28
Industrial applicability (IA)	Yes:	Claims	1-29
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

other multiple dependent claim.

3.3. To meet the requirements of Rule 5.1(a)(ii) PCT, the documents D1-D5 should be identified in the description and the relevant background art disclosed therein should be briefly discussed.

Re Item VIII.

4. The application does not meet the requirements of Article 6 PCT, because the claims, in particular the independent claims, are not clear.

4.1. Due to the wording of **claim 1**, the (abstract) features of the "detection channel" and the "flow path towards the detection channel" do not form part of the claimed "contactless detection cell". As a consequence, the feature "wherein the inner cross-section in at least a section of the detection channel is different than an inner cross-section of the flow path towards the detection channel" does not have any limiting effect on the claimed "detection cell", but rather appears to relate to a method of using said "detection cell". The scope for which protection is sought, hence, is rendered obscure.
In addition, it is not clear how said electrodes are arranged relative to said "detection channel".
Analogous objections are raised against **claims 16 and 17**.

4.2. **Claim 2** does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved ("... in a way that ..."), which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.
In addition, it is not clear what kind of "resistance" is meant (flow resistance ? / electrical resistance ?; see also **claim 27**).
Finally, it is not clear compared to what the said "resistance" should be increased.

4.3. In **claim 3**, the feature "axially separated" is indefinite since no axis has been defined previously.
The same deficiency arises in **claims 18 and 26**.

4.4. **Claim 4** does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved ("... sufficiently large for ..."), which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.
In addition, the feature "the axial separation" lacks antecedence.
Finally, it is not clear compared to what the said "cross-coupling" should be reduced.

4.5. The relative term "small" used in **claim 5** has no well-recognised meaning (at least in the context of an "inner cross-section of a detection channel") and leaves the reader in doubt as to the meaning of the technical feature/s to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).

4.6. The features "the respective sites of the detection channel" and "the portion between the electrodes" in **claim 6** lack antecedence.
The same applies to "the portion between the transmitter electrode and the receiver electrode" (**claim 8**), "the portion of the detection channel" and "the capillary" (**claims 9, 10**).

4.7. The feature in apparatus **claim 7** "... is axially varied ..." appears to relate to a method of using the apparatus rather than clearly defining the apparatus in terms of its technical features. The intended limitations are therefore not clear from this claim, contrary to the requirements of Article 6 PCT. A feature of actively varying the geometry of the detection channel is also not supported by the description and does not appear to have been intended.
To even further obscure the scope of said claim, an expression is used ("hour-glass shaped geometry") which does not appear to have a well-recognised meaning in the art.

4.8. In **claim 12**, the scope for which protection is sought (a detection cell *per se* ? / detection cell + detection channel ? / detection cell + detection channel + microfluidic chip device ?) is not at all clear (see also paragraph 4.1. above).

4.9. **Claim 15** does not contain any concrete apparatus feature limiting the claimed "detection cell", but rather appears to relate to a method of using said "detection

1. Reference is made to the following documents:

D1: US 2003/0222664 A1

D2a: M. Hanna *et al.*, "Novel three-dimensional capillary electrophoresis system for complex and trace analysis", J.Chromatogr. **A894** (2000) 117-128

D2b: A.J. Zemann *et al.*, "Contactless Conductivity Detection for Capillary Electrophoresis", Anal.Chem. **70** (1998) 563-567 (cited in D2a)

D3: US 2002/0067174 A1

D4: K. Mayrhofer *et al.*, "Capillary Electrophoresis and Contactless Conductivity Detection of Ions in Narrow Inner Diameter Capillaries", Anal.Chem. **71** (1999) 3828-3833

D5: WO 00/75650 A1

Re Item V.

2. The present application does not meet the criteria of Article 33(1) PCT, because, as far as it can be understood at all (see paragraph 4. below), the subject-matter of **claims 1-5 and 13-28** is not new in the sense of Article 33(2) PCT, and the subject matter of **claims 1-5, 9-16 and 18-28** does not involve an inventive step in the sense of Article 33(3)PCT.

2.1. Document **D1** (see in particular Fig.2,3 and description thereof) discloses (the references in parenthesis applying to this document) a contactless detection cell for detecting an electrical property of one or more sample compounds in a flow path (see title), said contactless detection cell comprising a transmitter electrode 18 adapted for capacitively coupling an AC current into a detection channel 24 of the flow path (§27 l.1,15-16, §30 l.14-18, §34 l.1-10); a receiver electrode 18 adapted for receiving the AC current that has been coupled into the detection channel 24 (§27 l.1,15-16, §30 l.14-18, §34 l.1-10); wherein the inner cross-section in at least a section of the detection channel is different than an inner cross-section of the flow path towards the detection channel (see Fig.2,3). Consequently, all features of **claim 1** are disclosed in D1 (Article 33(2) PCT).

2.2. Document **D2** (in D2a reference is made to D2b, see p.121 left-hand col. and p.128 right-hand col.) discloses a contactless detection cell for detecting an

electrical property of one or more sample compounds in a flow path (D2a: chapter 4.3., Fig.2: "Conductimeter 2"), said contactless detection cell comprising a transmitter electrode adapted for capacitively coupling an AC current into a detection channel of the flow path (D2b: Fig.1 and description thereof); a receiver electrode adapted for receiving the AC current that has been coupled into the detection channel (D2b: Fig.1 and description thereof); wherein the inner cross-section in at least a section of the detection channel is different than an inner cross-section of the flow path towards the detection channel (D2a: chapter 3.2.: "1st dimension: ... 800 µm I.D.; 2nd dimension: ... 300 µm I.D.").

Consequently, all features of **claim 1** are disclosed in D2 (Article 33(2) PCT).

As regards method **claim 22**, which steps correspond to the apparatus features of claim 1, it may be concluded, *mutatis mutandis*, that its subject-matter is also not new (Article 33(2) PCT).

2.3. Document **D2b** discloses a contactless detection cell for detecting an electrical property of one or more sample compounds in a flow path (Fig.1; p.564 left-hand col., §4), said contactless detection cell comprising a transmitter electrode adapted for capacitively coupling an AC current into a detection channel of the flow path (Fig.1; p.564, right-hand col., §3); a receiver electrode adapted for receiving the AC current that has been coupled into the detection channel (Fig.1; p.564, right-hand col., §3).

Document **D3** discloses (see Fig.1 and description thereof) a contactless detection cell for detecting an electrical property of one or more sample compounds in a flow path (see title), said contactless detection cell comprising a transmitter electrode 11 adapted for capacitively coupling an AC current into a detection channel 13 of the flow path (§18 l.7, §19 l.1-3, §20 l.3-5); a receiver electrode 12 adapted for receiving the AC current that has been coupled into the detection channel 13 (§18 l.8, §19 l.1-3).

Document **D4** discloses a contactless detection cell for detecting an electrical property of one or more sample compounds in a flow path (Fig.1 and description thereof), said contactless detection cell comprising a transmitter electrode adapted for capacitively coupling an AC current into a detection channel of the flow path (see "electrode 1" in Fig.1); a receiver electrode adapted for receiving the AC current that has been coupled into the detection channel (see "electrode 2" in Fig.1).

The subject-matter of independent **claim 1** differs from the disclosure of D2b, D3 or D4 only in that the inner cross-section in at least a section of the

detection channel is different than an inner cross-section of the flow path towards the detection channel.

The problem to be solved by the present invention may therefore be regarded as how to avoid or reduce cross-coupling between transmitter electrode and receiver electrode without compromising resolution and sensitivity.

When facing the above stated problem, the skilled person would consider the teaching of D5, which document, like D2b, D3 or D4, discloses a conductivity detection cell (see p.1 l.5-6). Although D5 does not disclose a contactless method, the cell of D5 is used with an alternative method, namely "potential gradient detection (see p.2 l.2-3, p.4 l.1-4). D5 clearly states (see p.15 l.16 - p.16 l.6, Fig.9) that while reducing the diameter of the detection channel, the distance between the two electrodes can be increased, as such resulting in a better electrical insulation between the two electrodes (see p.15 l.16-17). The resolution and sensitivity is said not to be compromised (p.15 l.20-21).

In view of D5, the solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT).

2.4. As regards method **claim 22**, which steps correspond to the apparatus features of claim 1, it may be concluded, *mutatis mutandis*, that its subject-matter is also not inventive (Article 33(2) PCT).

2.5. Dependent **claims 2-5, 9-21 and 23-28** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article 33(2) and (3) PCT) (see the citations given in the international search report).

2.6. The additional features of dependent **claims 6-8 and 29** do not appear to be disclosed or hinted at by the available prior art.

Re Item VII.

3.1. The independent claims are not in the two-part form in accordance with Rule 6.3(b) PCT.

3.2. Most of the dependent claims do not meet the requirements of Rule 6.4(a) PCT (3rd sentence), that multiple dependent claims shall not serve as a basis for any

cell". The scope for which protection is sought, hence, is rendered obscure (see also paragraph 4.1. above).

4.10. **Claim 17** contradicts claims 7, 8 and 16. This inconsistency leads to doubt concerning the matter for which protection is sought, thereby rendering the claims as a whole unclear (Article 6 PCT).

4.11. **Claim 21** should only refer to claims 19 and 20.

4.12. **Claims 22-29** do not appear to be supported by the description since a feature of actively reducing the inner cross-section of the detection channel (see independent claim 22) has no basis in the application documents (see also paragraph 4.7. above). It may be doubted whether claims related to a method are suitable at all in the present case.

4.13. Method **claims 24-29** should only refer to a method claim and not to "any of the above claims".

4.14. Furthermore, the claims are not concise, as required by Article 6 PCT.
Claim 18 comprises all the features of claim 1 and is therefore not appropriately formulated as a claim dependent on the latter (Rule 6.4 PCT).